REMARKS

In view of the following remarks, the Examiner is respectfully requested to withdraw the rejections and allow Claims 1-10 and 17-30, the only claims pending and currently under examination in this application.

Formal Matters

Claims 1-10 and 17-30 are pending after entry of the amendments set forth herein.

Claims 1-10 and 17-26 were examined. Claims 1-10 and 17-26 were rejected. No claims were allowed.

Claim 16 has been canceled as being directed to withdrawn subject matter.

Claims 1 and 17 have been amended. Support for the amendment can be found in the specification at, for example, page 9, lines 9 to 18 and page 9, lines 26 to 29.

New Claims 27-30 have been added. Support for the amendment can be found in the specification at, for example, page 9, lines 26 to 33.

As the above amendments introduce no new matter to the application, their entry is respectfully requested.

Withdrawal of Objections

The Applicants express gratitude in the Examiner's indication that objections not repeated from the Office Action dated June 1, 2005, have been withdrawn.

Certification Regarding Sequence Listing

I hereby certify that the enclosed Sequence Listing is being submitted under 37 CFR §§ 1.821(c) and (e) in paper and computer readable form (Compact Disk labeled 'CRF').

As required by 37 CFR 1.821(f), I hereby state that the content of the paper and computer readable copy of the Sequence Listing, submitted in accordance with 37 C.F.R. §1.821(c) and (e) are the same. The Computer Readable Format (CRF), being submitted under 37 CFR §§ 1.52(e) and 1.824, is formatted on IBM-PC, the operating system compatibility is MS-Windows and the file listing is:

Seqlist.txt 29 KB created April 12, 2006.

I hereby certify that the enclosed submission includes no new matter. The Sequence Listing was prepared with the software FASTSEQ, and conforms to the Patent Office guidelines. Applicant respectfully submits that the subject application is in adherence to 37 CFR §§ 1.821-1.825.

Priority

The Office Action maintains that the non-provisional application 09/976,673 does not provide support for nucleic acid molecules encoding a polypeptide product comprising a first and second chromo/fluorescent domain that are form Cnidarian species.

The Applicants maintain that non-provisional application 09/976,673, discloses a nucleic acid encoding a polypeptide product comprising a first and a second chromo/fluorescent domain, where the nucleic acid coding elements **are form *Cnidarian* species**.

Non-provisional application 09/976,673 provides on page 35, lines 24-29, and Figures 12 and 13, a working example describing a nucleic acid encoding the polypeptide Cr-44-9. The Cr-44-9 polypeptide comprises a first and a second chromo/fluorescent domain as required by Claim 1 of the present application. Moreover, as noted on page 17, lines 10 to 16, the chromo/fluorescent domains are derived from Heteractis crispa, which is a *Cnidarian* species.

As shown in Figure 12, nucleic acid residues 1 to 697 of SEQ ID NO:15 **encode the first chromo/fluorescent domain** derived from Heteractis crispa (corresponding to amino acids residues 1 to 228 of SEQ ID NO:16), and nucleic acid residues 710 to 1396 of SEQ ID NO:15 **encode the second chromo/fluorescent domain** derived from Heteractis crispa (corresponding to amino acids residues 233 to 460 of SEQ ID NO:16). The Cr-44-9 polypeptide comprises a first and a second chromo/fluorescent domain as required by Claim 1 of the present application. Therefore, the disclosed nucleic acid

encoding the Cr-44-9 polypeptide is within the genus of claimed nucleic acids in the present application.

Objection to the Specification

The specification has been objected to for containing sequences without sequence identification numbers. The specification has been amended on pages 3 and 39 to include sequence identification numbers. Accordingly, this objection may be withdrawn.

Rejection under 35 U.S.C. § 112, first paragraph (Enablement)

Claims 1-10 and 17-26 have been rejection under 35 U.S.C. §112, first paragraph, for allegedly failing to provide enablement for all nucleic acid encoding polypeptide products comprising a first chromo/fluorescent domain and second chromo/fluorescent domain, wherein the first and second chromo/fluorescent domains are oligomeric and oligomerize under intracellular conditions so that the polypeptide assumes a tertiary structure. In view of the remarks made herein, this rejection is respectfully traversed.

As noted in the Office Action, a specification complies with the statute even if a reasonable amount of experimentation is required, as long as the experimentation is not "undue". One way to determine if undue experimentation is required is to utilize the *Wands* factors.[1] However, all of the factors need not be reviewed when determining whether a disclosure is enabling.[2]

The Applicants respectfully submit that when evaluated in view of the relevant *Wands* factors, the specification clearly enables one of skill in the art to practice the subject invention without undue experimentation. In other words, Claims 1-10 and 17-26 contain subject matter which is adequately described in the specification in such a way

1 (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims

to teach someone how to make and use the claimed invention without having to practice undue experimentation.

The Applicants note that the courts have clearly taught that the fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation (see also MPEP §2164.01).[3]

The claims of present application are directed to nucleic acids that encode a polypeptide product comprising a first chromo/fluorescent domain linked by a linking domain to a second chromo/fluorescent domain, wherein the first and second chromo/fluorescent domains oligomerize under intracellular conditions to assume a tertiary structure. As provided below, the Applicants maintain that the specification provides ample disclosure to enable one skilled in the art to practice the claimed invention.

For example, the subject nucleic acids are described, for example, on page 9, line 3 through page 17, line 15; the particular linked chromo/fluorescent domains aspect is described, for example, on page 10, line 18 though page 12, line 7; exemplary methods of producing such nucleic acids are described, for example, on page 37, line 19 through page 39, line 18; resulting exemplary nucleic acids encoding linked chromo/fluorescent domains are described at, for example, on page 37 and Figures 1-5; constructs, vectors, expression cassettes, and expression systems including the subject nucleic acids are described, for example, on page 15, line 16, through page 17, line 25; and applications using the subject proteins are described, for example, on page 28, line 17, though page 36, line 20.

In addition, the present application contains working examples demonstrating exemplary protocols for generating the subject nucleic acids encoding polypeptides

---

2 See *Amgen, Inc. v. Chugai Pharm. Co.*, 927 F.2d 1200, 1213, 18 USPQ2d 1016, 1027 (Fed. Cir. 1991).
3. See also *In re Certain Limited-Charge Cell Culture Microcarriers*, 221 USPQ 1165, 1174 (Int'l Trade Comm'n 1983), *aff'd sub nom.*, *Massachusetts Institute of Technology v. A.B. Fortia*, 227 USPQ 428 (Fed. Cir. 1985).

having linked chormo/fluorescent domains (pages 38 and 39), at least four exemplary nucleic acids are provided, including Cr-44-9 (SEQ ID NOs: 1 and 2), HcRed-cr-1 (SEQ ID NOs: 5 and 6), AsRed-35-5NA (SEQ IN NOs: 7 and 8), AsRed-35-5D (SEQ ID NOs: 9 and 10) (page 37 and Figures 1-5), and exemplary methods of evaluating such polypeptides having linked chormo/fluorescent domains suitable for use with the subject invention (pages 38 and 39). As such, the present application does provide a person skilled in the art, through the specification as well as the working example, sufficient enablement for the subject invention.

Furthermore, the Applicants note that the presence or absence of working examples is but one factor to be taken into consideration in determining whether the specification is enabling for the full scope of the claims. Under MPEP § 2164.02 the consideration is whether one skilled in the art would be expected to be able to extrapolate the provided examples across the entire scope of the claim. As presented herein, Applicants argue that it would be reasonable to conclude that one skilled in the art would be able to extrapolate the working examples provided in the specification across the entire scope of the claims without excessive and undue experimentation. As such, based on the disclosure provided in the application one skilled in the art would be able to extrapolate the working examples to the full scope of the pending claims.

In maintaining this rejection, the Office Action has focused on the scope of the claims and asserts that the specification does not enable any polypeptides. However, as detailed above, the specification describes multiple different species of fluorescent proteins from *Cnidarian* species. In addition, the specification also describes in great detail several examples of such nucleic acids, including Cr-44-9 (SEQ ID NOs: 1 and 2), HcRed-cr-1 (SEQ ID NOs: 5 and 6), AsRed-35-5NA (SEQ IN NOs: 7 and 8), AsRed-35-5D (SEQ ID NOs: 9 and 10) (page 37 and Figures 1-5).

The Office Action also cites several references as casting doubt with respect to the enablement of the present invention. The Applicants respectfully disagree. The references cited in the Office Action are directed to either hybrid gene encoding a fusion

protein of the N-terminal part of dsFP593 and the C-terminal part of drFP583 (Fradkov et al.) or the oligomerization properties of DsRed (Baird et al.). Therefore, the cited references do not provide any support for the position that the present invention is not enabled *because they provide no disclosure as to why the claimed invention would not work as described in the present application.* In addition, the references cited in the Office Action do not cast doubt as to the enablement of the claimed invention because the applicants have successfully shown specific examples that have the recited properties.

Constructing a nucleic acid encoding a polypeptide having a first chromo/fluorescent domain linked by a linking domain to a second chromo/fluorescent domain is routine and can be performed by one having skill in the art without unnecessary experimentation. Since the specification actually provides several examples of nucleic acids encoding such polypeptides, there is no reason to think that this would not work for all such fluorescent proteins.

In sum, the amount of experimentation required to subject invention would not be undue and excessive because working examples have been provided, guidance is given on how to generate such nucleic acids, and one of skill in the art would be able to perform the experiments as a matter of routine. The specification therefore provides sufficient enablement such that one of ordinary skill in the art would be able to practice the invention without undue experimentation. Accordingly, the specification clearly enables the subject invention as demonstrated in view of the relevant *Wands* factors.

As such, for at least the reasons described above, Claims 1-10 and 17-26 are adequately enabled by the specification. Accordingly, the Applicants respectfully request that the rejection of Claims 1-10 and 17-26 under 35 U.S.C. §112, first paragraph be withdrawn.

Rejection under 35 U.S.C. § 112, second paragraph

The Office Action has rejected Claims 1-2 and 17 under 35 U.S.C. § 112, second paragraph for allegedly failing to particularly point out and distinctly claim the subject matter regarded as the invention. In particular, the Office Action states that "it is not clear how the applicants envision the domains of the peptide to oligomerize in order to form a protein complex, which assumes a particular tertiary complex" (Office Action, page 14). In view of the amendments to the claims, this rejection may be withdrawn.

As provided in greater detail in the specification on page 9, the tertiary structure of the encoded polypeptide is a result of the oligomerization of the first chromo/fluorescent domain and the second chromo/fluorescent domain. The resulting tertiary structure of the polypeptide is an oligomeric tertiary structure.

In the spirit of expediting prosecution and without conceding to the correctness of the rejection, Claims 1 and 17 have been amended for clarity to recite that the first and second chromo/fluorescent domains are "**linked by a linking domain**" and that the "encoded polypeptide assumes a **linked oligomeric** tertiary structure".

In view of the amendments to the claims, the Applicants respectfully request that this rejection be withdrawn.

Rejection Under 35 U.S.C. § 102

The Office Action has rejected Claims 1-5, 7-10, 17-21, and 23-26 under 35 U.S.C. § 102(b) for allegedly being anticipated by Fradkov et al., (FEBS Lett. 479:127-130 (2000)) as evidenced by Matz et al., (Nature Biotech. 17:969-973 (1999)). In view of the amendments to the claims, this rejection may be withdrawn.

The present claims are directed to nucleic acids encoding polypeptides comprising a first chromo/fluorescent domain a second chromo/fluorescent domain. As noted above, Claims 1 and 17 have been amended to recite that the first and second chromo/fluorescent domains are "**linked by a linking domain**".

In contrast, Fradkov et al. discloses a fusion protein including the N-terminal part of the dsFP593 and the C-terminal part of the drFP583 (page 139, third paragraph). Fradkov et al., does not teach a linking domain linking the two portions of the fusion protein.

As such, since the cited reference fails to teach a "linking domain", the cited reference fails to teach each and every element as found in the claims. Therefore, the Applicants respectfully request that this rejection be withdrawn.

Rejection Under 35 U.S.C. § 103

The Office Action has rejected Claims 1, 6, 18, and 22 under 35 U.S.C. § 103(a) for allegedly being unpatentable over Fradkov et al., as evidenced by Matz et al., in view of WO 01/127150. In view of the amendments to the claims, this rejection may be withdrawn.

As noted above Fradkov et al. fails to disclose a first chromo/fluorescent domain linked by a linking domain to a second chromo/fluorescent domain. Since WO 01/127150 has been cited for teaching a nucleic acid encoding a fusion protein comprising a chromo/fluorescent domain fused to a non-chromo/fluorescent protein domain, WO 01/127150 fails to make up the deficiency of Fradkov et al.

Therefore, since the cited references fail to teach a "linking domain", the cited alone or in combination fail to teach each and every element found in the claims. As such, the Applicants respectfully request that this rejection be withdrawn.

CONCLUSION

In view of the above remarks, this application is considered to be in good and proper form for allowance and the Examiner is respectfully requested to pass this application to issuance.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815.

Respectfully submitted,
BOZICEVIC, FIELD & FRANCIS LLP

Date: April 26, 2006 By: _____
Edward J. Baba
Registration No. 52,581

Date: April 26, 2006 By: _____
Bret E. Field
Registration No. 37,620

BOZICEVIC, FIELD & FRANCIS LLP
1900 University Avenue, Suite 200
East Palo Alto, CA 94303
Telephone: (650) 327-3400
Facsimile: (650) 327-3231
F:\DOCUMENT\CLON\094\response to office action of 1-27-06.DOC